Cancer Research Center Hotline

Childhood Cancer Rapid Changes in the Last 40 Years

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Over the last 40 years we have witnessed a dramatic improvement in the survival of children with cancer. Today, 75-80% of children diagnosed with childhood cancers can expect to be long-term survivors. Childhood cancer is an uncommon phenomenon with approximately one in 7000 children being diagnosed each year. Today, we can expect that 12,400 children under 20 years of age will be stricken with cancer in the United States each year. The incidence of childhood cancer has increased only slightly over 40 years. This is thought to be due to environmental exposures in certain young age groups with increases in leukemia, germ cell tumors and brain tumors. Fifty percent of childhood cancers still occur in the form of acute leukemias and lymphomas with another 25% being attributed to brain tumors. The remaining 25% is caused by Wilms' tumor, osteogenic sarcoma, neuroblastoma and germ cell tumors.

Each type of cancer has shown a dramatic improvement in survival except for childhood neuroblastoma, infant leukemia and brainstem tumors. The dramatic improvement in survival is a blueprint and guiding light for other problem areas in medicine. Success has been attributed to many things, which include the emergence of multidisciplinary children's cancer centers, improvement in diagnostic technologies, the availability of pediatric subspecialists, antimicrobials and other supportive care, but more so the collaborative efforts of clinicians participating in clinical trials.

In the 1960s and 1970s, clinicians formed the Children's Cancer Group and the Pediatric Oncology Group and designed clinical trials for each common pediatric malignancy. Participation in these trials was almost universal by the early 1990s when most of the children with malignancies were registered on a clinical trial. In the year 2000, all of the cooperative children's groups in the country merged into the Children's Oncology Group with almost 300 member institutions.

Prior to 1970, the cure rate for acute lymphoblastic leukemia (ALL) was virtually zero. With total aggressive therapy and prophylactic central nervous system treatment, the group at St. Jude's demonstrated that nearly 50% of children with ALL could be cured in 1970. Today, that figure has risen to 80-90%, and some subgroups of low risk ALL can expect a 99% cure rate. Equally dramatic has been the improved survival of children with non-Hodgkin's lymphoma, Wilms' tumor, osteogenic sarcoma, rhabdomyosarcoma and subgroups of brain tumors. The key to all of this success seems to be the aggressive surgical therapy when needed, radiation therapy with state-of-the-art equipment, and application of the most aggressive courses of chemotherapy developed from evidence-based medicine trials.

Great strides have been made in epidemiological research in childhood cancer over the last 30 years. The United States has an exceptionally high quality cancer surveillance system begun in 1973 and funded and compiled by the National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) Program that has collected extremely important data. Fourteen percent of the U.S. population is included in this data and more than 30,000 cases of malignant neoplasms in children under 19 years of age.

A number of important case control studies have been done looking at low frequency electromagnetic fields (EMF), and to date no association between EMF exposure and various childhood cancers has been found. Other studies have tried to link childhood cancer with feline and other mammalian leukemias; highly processed foods, such as hot dogs; dietary supplements; viruses; immunizations; and a number of medications, all unsuccessfully.

When a child is diagnosed with cancer, the family frequently asks if there is a hereditary cause for the malignancy. Overwhelming evidence demonstrates that cancer is the result of multiple mutations in the DNA of tumor cells. In contrast to the predominant systematic mutation, the proportion of pediatric cancers that have a clearly hereditary component is small. A child, therefore, may have a hereditary predisposition to cancer with a negative family history because of a constitutional chromosome disorder, such as Down's syndrome or a de novo mutation in a cancer predisposing gene such as Rb. Several pediatric tumors have been identified to have a hereditary component, i.e., adrenal cortical carcinoma, optic glioma, retinoblastoma, pheochromocytoma, Wilms' tumor, central nervous system neoplasms, and some leukemias. This genetic tendency is hereditary as it can range from 1-10% depending on the type of malignancy. Wilms' kidney tumor is associated with multiple genetic syndromes, including some chromosomal deletion syndromes, an autosomal dominant disorder and a syndrome resulting from disruption of imprinting.

One of the most striking predispositions to cancer caused by a constitutional chromosome abnormality is increased leukemia in children who have trisomy-21 (Down's syndrome). This risk is almost three percent over a 30-year period. An increased risk of cancer is seen in children with Klinefelter's syndrome, Turner's syndrome, WAGR's syndrome, Beckwith-Wiedemann's syndrome and neurofibromatosis, hereditary telangiectasia, von Hippel-Lindau's disease, and many other genetic conditions and familial disorders. At the present time, it is important for pediatric oncologists to recognize patients and families that may have a familial genetic cancer and refer them to a geneticist/genetic counselor. Recently, a multidisciplinary approach taken by several groups involving pediatric oncologists, clinical geneticists, genetic counselors and psychologists has been to form referral groups to address these problems.

The molecular basis for childhood cancer has been under intense study in pediatric groups. The search for a molecular basis has been arduous and frustrating, but the DNA of cancer cells is different. Cancer cells carry within their DNA point mutations, viral insertions or gene amplifications, deletions or gene rearrangement, each of which can alter the context and process of normal cellular growth and development.

Identification and characterization of the involved genes and of the mechanism by which they can be altered, provide basic insight into the process of carcinogenesis and offer the hope of specific therapies if the alteration or its effect can be stymied or reversed. For the first time we have inserted into our vocabulary the idea of rehabilitating cancer cells rather than killing these wayward cells. The discovery of key molecular events in the pathogenesis of childhood tumors has not translated into major advances in therapy but evidence from many fronts, including the treatment of acute promyelocytic leukemia (APL) with an all trans-retinoic acid, suggests that cancer will eventually yield to molecular interventions.

The biology of childhood cancers has become quite complex, and we have found that cells have developed signal transduction pathways that enable them to sense and respond to neighboring cells and their extracellular milieu. These signaling pathways influence survival/death, growth/growth arrest, differentiated/undifferentiated, motile/non-motile, and angiogenic/anti-angiogenic decisions, and ultimately cell fate. Components of these pathways include membrane-bound protein receptors, cytoplasmic/nuclear receptors, phospholipid signaling systems, and ion channels. Understanding of all of these complexities will afford new avenues for therapy in the future.

The area of tumor immunology in pediatric cancer is slowly evolving but is still in its infancy stage. Integrating immunologic strategies with chemotherapy, cell modulation, surgery and radiation are future goals of pediatric oncologists.

Newer areas for pediatric oncologists include prevention of pediatric malignancies and preventing and managing some of the long-term consequences of therapy. Educational issues, care of a dying child, financial issues, advocacy, insurance, and employment discrimination are being addressed. The role of complementary therapy and alternative medical therapy along with outreach to Third World countries is rapidly evolving. It seems in pediatric oncology that "we are no longer at the beginning nor at the end, but certainly at the end of the beginning." There are many problems and issues to address in the future, but with the resources available and willingness to work together, our goal is still to cure every child with cancer.

For more information visit the Cancer Research Center's website at www.crch.org or call the Cancer Information Service of Hawaii at 1-800-4-CANCER.